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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/501,171	02/09/2000	Peter George-Hyslop	1034/1F811-US1	3487

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Darby & Darby P.C.
805 Third Avenue
New York, NY 10022

EXAMINER
TURNER, SHARON L

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/501,171	GEORGE-HYSLOP ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *14* is/are allowed.

6)☒ Claim(s) *3,4 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3-11-03 has been entered.

2. The amendment filed 11-7-02 has been entered into the record and has been fully considered. Claims 2 and 5-13 are canceled. Claims 3-4 and 14-15 are pending.

3. As a result of applicants amendment, all rejections not reiterated herein have been withdrawn by the examiner.

Election/Restriction

4. Applicant's election without traverse of Group I, in Paper No. 9 is acknowledged.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-4 and 15 are rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for the induction of cellular extensions in neuronal cells via contacting with SEQ ID NO:4, does not reasonably provide enablement for induction of cellular extensions in any cell type as generically claimed in claim 3 or for

providing neuronal regeneration as claimed in claim 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants argue with respect to the new claims that the specification at p. 3, lines 6-15, p. 4, lines 11-16, p. 5, lines 16-24, p. 6, lines 1-8 and p. 7, lines 24 to p. 8, line 2 support the enablement within the skill in the art for the claimed invention and that any experimentation required would not be undue. Applicants argue that Skolnick is not particularly relevant to the art of nerve growth and that the non-enabled embodiments are not of interest.

Applicant's arguments filed 3-12-02 have been fully considered but are not persuasive.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

The specification at p. 3, lines 6-15 states that the invention describes methods of inducing neurite outgrowth via contacting with hNPRAP. At p. 4, lines 11-16 the specification states that "over-expression of hNPRAP, or functional derivatives thereof containing one or more armadillo repeats, causes the development of numerous long, dendritic processes which typically terminate upon distantly located cells," and that "the hNPRAP induced cellular extensions are highly similar to the axonal sprouting seen

during neuronal regeneration and synapse formation." The specification at p. 6, lines 1-8 further teach stimulating outgrowth by contact with agents that induce hNPRAP expression or delivery via viral vectors. Pages 7, lines 24-p. 8, line 2 teach that assays for measuring sprouting of axons of neuronal cultures or dendrite formation in non neurological cells are well known in the art.

Yet, the specification fails to exemplify any other type of cells (as encompassed by generic claim 3) that exhibit cellular extension or outgrowth upon contact with hNPRAP. The specification specifically fails to exemplify that non-neuronal cells respond. Similarly, the specification fails to exemplify that over-expression via either vector induced expression or administration of hNPRAP modulating molecules induces cellular extensions within any non-neuronal cell types.

Moreover, the specification fails to show any exemplary evidence of "neuronal regeneration" or synapse formation by contact with the hNPRAP peptides of SEQ ID NO:4 as claimed in claim 4. As noted by Jackowski et al., Br. J. of Neurosurg., 9:303-317, 1995, neuronal cells and especially CNS neuronal cells differ from other cell types as neurons are inhibited in regenerative capacity. Peripheral and central nerve regeneration are processes in which the relative success or failure of the event relies on the combined effects of a number of neuronal and non-neuronal events including the cellular and extracellular matrix, neurotrophic factors, the rate and efficiency of elongation and the specificity of target reinnervation amongst others, see in particular p. 31, paragraph 1 in Liuzzi et al., Neurosurg. Clin. of N.Am., 2(1):31-42, 1991. While such unpredictability is noted, the specification including at p. 3, lines 6-15, p. 4, lines

11-16, p. 5, lines 16-24, p. 6, lines 1-8, p. 7, lines 24 to p. 8, line 2, fail to teach a single exemplary embodiment where neuronal regeneration is is achieved with a hNPRAP peptide of SEQ ID NO:4 as directed in Applicant's claims. In particular, Luizzi notes that neuronal regeneration is the culmination of multiple events that allows targeting and functional signalling amongst neuronal cells. Thus, the specification's teachings noting the induction of celluar extensions fails to evidence neuronal regeneration via either contacting or over expression of the disclosed hNPRAP peptide of SEQ ID NO:4.

Thus, based on the specifications limited observations and a lack of experimental data the skilled artisan would fail to find the specification's evidence indicative of neuronal regeneration or synapse formation as claimed. Moreover, the artisan would not be apt to expect such effects based merely upon the promotion of cellular extensions. No exemplary evidence is provided and the references noted above would lead the artisan to doubt a necessary correlation between process outgrowth (celluar extensions) and "neuronal regeneration" as claimed. Moreover, while the specification appears to contemplate the use of the molecule to induce cellular extensions in non-neurological cells, Applicant's have not apparently observed such extensions in non-neurological cells nor have Applicant's noted the significance or use associated with providing cellular extensions in such non-neurological cells.

The specification states at p. 4, lines 23-27 that hNPRAP is known to interact with Presenilin I and II and that the domain of the PSI protein that interacts with hNPRAP has also been shown to interact with other proteins such as armadillo repeat proteins, p0071 and beta-catenin, hNPRAP presumably being of such a family and

merely requiring the armadillo repeats for the stimulation of neuronal regeneration and axon sprouting, specification p. 5, lines 16-28.

However, as taught by Paffenholz et al., (IDS) the plakoglobin/armidillo multigene family is made of a growing number of very different proteins which are divergent in function and independent in structure from each other, see in particular Introduction, p. 293-294. Paffenholz et al., clearly recognizes armadillo repeat proteins, but fail to recognize neuronal regeneration as a function of such proteins. Moreover, the skilled artisan readily recognizes the unpredictable nature of protein chemistry. As noted by Skolnick et al., Trends in Biotech., 18(1):34-39, 200 even in highly related protein families, structural modifications by even a single amino acid substitution may lead to functional changes in biological activity, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000. Further, Tanahasi et al., Neuroreport, 10:563-568, Feb. 25, 1999 (a post-priority date reference) discloses delta-catenin that exhibits 100% identity with instant SEQ ID NO:4. However, the reference fails to note or distinguish the peptide as a neuronal regeneration factor and there is no further pre- or post-filing date evidence to support the hNPRAP molecule of SEQ ID NO:4 as exhibiting such activities in non-neuronal cells.

Thus, without further undue experimentation the skilled artisan could not make and use the full scope of the claimed invention.

Status of Claims

6. Claim 14 is allowed.

Conclusion

7. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon Turner

Sharon L. Turner, Ph.D.
June 13, 2003